# IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

MAY 1 2 2003

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In re the application of: Curtis, Rory A.J.

Serial No.: 09/587,111

Filed: June 2, 2000

For: NOVEL MEMBERS OF THE CAPSAICIN/VANILLOID RECEPTOR FAMILY OF

PROTEINS AND USES THEREOF

Attorney Docket No.: MNI-062CP2DV1

Commissioner for Patents

Box AF

Washington, D.C. 20231

Group Art Unit: 1646

Examiner: Ulm, J. D.

Certificate of Facsimile Transmission

I hereby certify that this correspondence is being facsimile transmitted to the Commissioner for Patents, Box AF, Washington, D.C. 20231 on the date set forth below.

By:

**Date of Signature** 

María Laccotripe Zacharakis, Ph.D.

**Attorney for Applicant** 

Limited Recognition Under 37 C.F.R. 10.9(b)

# **DECLARATION PURSUANT TO 37 CFR §1.131**

Dear Sir:

I, Rory A.J. Curtis, a citizen of the United Kingdom, residing at 78 Hardwick Road,

Ashland, Massachusetts 01721 hereby declare as follows:

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- (1) I am the inventor of the subject matter described and claimed in the above-identified application.
- (2) Prior to January 22, 1999, the invention described and claimed in the abovereferenced patent application was completed in this country, as evidenced by the following:
- (a) Prior to January 22, 1999 I had completed the sequencing of the full length human VR-2 (SEQ ID NO:5) as evidenced by copies of the assembled contig map and the complete sequence of SEQ ID NO:5 derived from the contig map. The contig map and sequence print-out are submitted herewith as Exhibits A and B, respectively.
- (b) Prior to January 22, 1999 I had determined that the polypeptide of SEQ ID NO:5 was a vanilloid receptor based on the results of a blast search using the amino acid sequence of SEQ ID NO:5. The top hit in this blast search analysis is rat vanilloid receptor 1 (VR-1; accession number AF029310). Based on the percent identity and percent similarity between the polypeptide of SEQ ID NO:5 and rat VR-1, and the fact that rat VR-1 was the top hit in the blast search analysis I determined that the polypeptide of SEQ ID NO:5 was a vanilloid receptor. The results of the blast search analysis are submitted herewith as Exhibit C.
- (c) Prior to January 22, 1999, I had determined that the polypeptide of SEQ ID NO:5 represents a unique target for pain and that it may be responsible for hypersensitivity in chronic neuropathic pain, as evidenced by a copy of the "Qualified Target Summary Sheet" generated for this molecule. The Qualified Target Summary Sheet is submitted herewith as Exhibit D.

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(d) According to my routine practice, immediately after identifying the polypeptide of SEQ ID NO:5 as a vanilloid receptor (hVR-2) associated with pain and classifying it as a Qualified Target, I contemplated routing uses of this molecule such as: (i) use of the molecule in screening assays to identify modulators of the vanilloid receptor or (ii) use of this molecule in the diagnosis of conditions/diseases associated with, for example, aberrant vanilloid receptor (hVR-2) nucleic acid expression or activity, e.g., pain disorders, as evidenced by a copy of the "Qualified Target Summary Sheet" generated for this molecule.

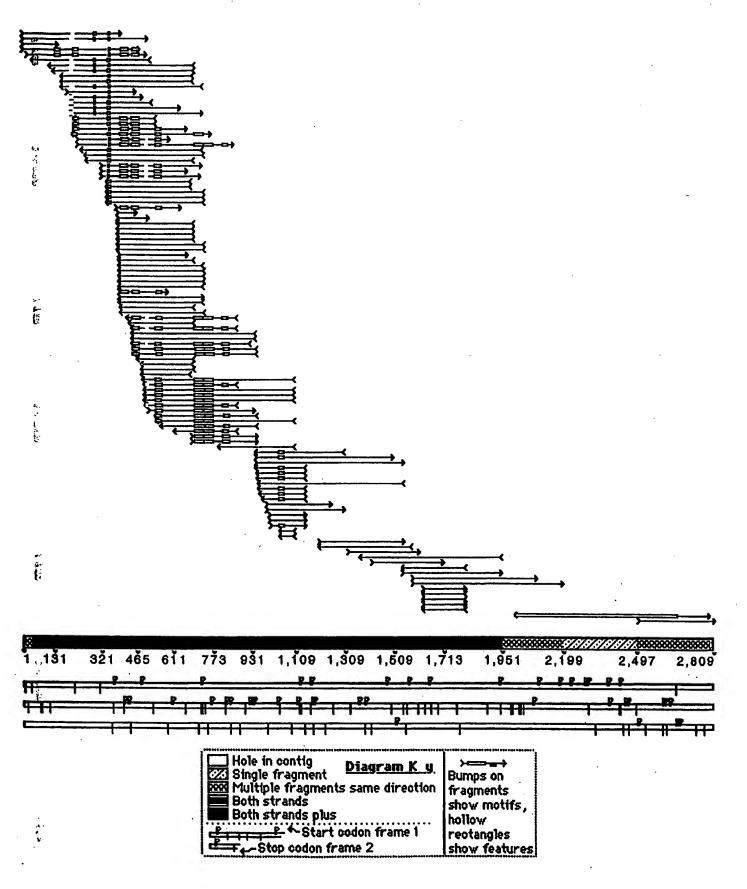
(e) The dates deleted from the contig map (Exhibit A), the sequence print-out (Exhibit B), the blast search results (Exhibit C), and the Qualified Target Summary (Exhibit D) are prior to January 22, 1999.

I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements are made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of this Application for Patent or any patent issuing thereon.

Long Cords

10/2003

21e11a Sequencher™ "21e11racefinal"



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🔁 £1hx11e11r19a2 | 18 GATTINGGAA GCGGGCTGCC TCCCATGAAG TCNCAGTTCA AGGGCGAGGA CCGGAAATTC GCCCCTCAGA TAAGAGTCAA CCTCAACTAC
A Elbx21611x1941 48 GATTTGGGA GCGGGCTGCC TCCCATGAAG TCACAGTTCC AGGGCGAGGA CCGGAAATTC GCCCCTCAGA TAAGAGTCAA CTTCAACTAC
Gerbank Aliza. 16 GATTTTGGGA GCGGGCTGCC TCCCATGGAG TCACAGTTCC AGGGCGAGGA CCGGAAATT
                                                                                         CTCAGA TAAGAGTCAA CCTCAACTAC
Stimal 13-242 13 GATTTINGGA NCGGGCTGCC TCCCATGHAG TCACAGTTCC AGGGCGAGGA CHGNAAATTC GCCCCTCAGA TAAGAGTCAA CCTCAACTAC
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[3] jthea103e2x1	<b>M1</b> ×	ጥሞጥርርር ል	GCGGNCTGCN	TCCCATCMAG	<b>サクシウン ひをすぐぐ</b>	AGGNCGAGGA	CCGNALATTC	accommon a n	TARGROWER.	CCECNACENC
		1110001	000011010011	1 CCCN 1 GMAG	ICACAGIICC	MOUNTONOON	COMMITTE	accent cada	INNUNUTURC	CCTCAACTAC
Elb21011r18			TGCC	TCCCATGGAG	TCACAGTTCC	AGGGCGAGGA	CCGGAAATTC	GCCCCTCAGA	TAAGAGTCAA	CCTCAACTAC
A 6110021-0111721				AG	TCACAGTTCC	AGGNCGAGGA	CCGGAAATTC	GCCCCTCAGA	TAAGAGTCAA	CCTCAACTAC
2 11b0101011r17				AG	TCACAGTTCC	AGGGCGAGGA	CCGGAAATTC	GCCCCTCAGA	TAAGAGTCAA	CCTCAACTAC
Stinc31011x33"	<b>&gt;#1&gt;</b>				TCACAGTTCC	AGGGCGAGGN	CCGGAAATTC	GCCCCTCAGA	TAAGAGTCAA	CCTCAACTAC
Elbelelleri	>#1>			•	TCC	A: GGCGAGGN	CGGAAATTTC	NCCCNTCAGA	TARARGTCAC	CCTCAACTNC
Genbank AA4	>#1>					AGGGCGAGGA	CCGGAAATT	CTCAGA	TAAGAGTCAA	CCTCAACTAC
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Aflhx21e11rrl	>#1>					GGGCGAGGA	CCGGAAATTN	GCCCNTCAGA	TAAGAGTCAA	CCTCAACTAC
Aflhx21e11rrl						GGC : AGG :	NCGGAAATTC	GCCCTCAAA	TAA: AGTCAA	CCTCAACTNC
Gembank AA8						GGA	CCGGAAATT	CTCAGA	TAAGAGTCAA	CCTCAACTAC
Genbank AA2							TC	GCCCCTCAGA	TAAGAGTCAA	CCTCAACTAC
🗿 jthsa103e2w1	>{1>									TAC
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#451 GATTTTGGGA GCGGGCTGCC TCCCATGGAG TCACAGTTCC AGGGCGAGGA CCGGAAATTC GCCCCTCAGA TAAGAGTCAA CCTCAACTAC D F G S G L P P M E S Q F Q G E D R K F A P Q I R V N L N Y

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¥	f1bxc21e11g2	8400									
¥	flhxc21e11g1	#428	CGAAAGGGAA	CAGGTGCCAG	TCAGCCGGAT	CCAAACCGAT	TTGACCGAGA	TCGGCTCTNC	AATGCGGTCT	CCCGGGGTG	r ccccgaggat
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16	9 cresco 1911513"	#380	CGAAAGGGAA	CAGGTGCCAG	TCAGCCGGAT	CCAAACCGAT	TTGACCGAGA	TCGGCTCTTC	AATGCGGTCT	CCCGGGGTGT	CCCCGAGGAT
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	jthsa103e2b2	#332	CGAAAGGGA								
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A			CGAAAGGGAA	CAGGTGCCAG	TCAGCCGGAT	CCAAACCGAT	TTGACCGAGA	TCGGCTCTTC	AATGCGGTCT	CCCGGGGTGT	CCCCNAGGAT
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12	flh%21e11rrl	<b>#</b> 161	CGAAAGGGAA	CAGGTGCCAG	TCAGCCGGAT	CCAAACCGAT	TTGACCCAGA	TCGGGTCTTC	AATGCNGTCT	CCCGGGGTGT	LCCCGAGGAT
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_	flhx21e11r17_		CGAAAGGGAA	CAGGTGCCAG	TCAGCCGGAT	CCAAACCGAT	TTGACCGAGA	TCGGCTCTTC	AATGCGGTCT	CCCGGGGTGT	CCCCGAGGAT
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=			CGAAAGGGAA	CAGGTGCCAG	TCAGCCGGAT	CCAAACCGAT	TTGACCGAGA	TCGGCTCTTC	AATGCGGTCT	CCCGGGGTGT	CCCCGAGGAT
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17	flhi21e11r17g1	#63	CGAAAGGGAA	CAGGTGCCAG	<b>ም</b> ፈ የአይጋጓን ይፈ ጓሞ	CCABACCCAS	MMO2000202	******			
R	flhx21e11r22g2 flhx21e11rr12	<b>#</b> 61	CHARAGGGAA	CAGGTGCCAG 4	TCAGCCGGAT	CCAAACCGAM	STEC ROOM OR	maaaaaaaa			
			COUNTY ! GGWU	CHOOLCCCMG	CAGCOGGAT	CCAAACCGAT	TNGACCGAGA	TCGGNTTTTC	<b>ልእ</b> ፕሮርርርጥጥሮም <i>(</i>	TOGGOOGTOT	CCCCGROONE
R	rmwrerfffff)"	#2T	CGAAAAGGAA	CAGGTCCCAG	TCACCCGGNT	CNAAACCGAT	TTGACNGAGA :	TCGG: TTTTC	AATCGGGTCT (	CONGGGGTGT	CCCCGAGGAT
3	flb#21011rr13	<b>\$</b> 50	AADDDAAADM	CAGGTGCCAG	TCA: NCGGAT	CC: AANC AT	TTGACCGAGA	TCGGCTCTTC	AATCGGTTCT (	CCGGGGGTGT	CCCNGAGGAT

Ċ	<b>\$</b> 541	CGA	LAG	GGAI	C.	AGGT	GCCAG	TCA	gcc p	GGAT	CCI		CGAT			GAGA R D			_	AAT	GCC	GTC	T			'GT	ccc	CGA	GGAT	
Genbank AIO	>#1>																					c	T	ccce	3 <b>G</b> G1	'GT	ccc	CGA	GGAT	1
1thsa103e2x2																								ccce						
2f1bx21e11rr9		AF					GCCAG																							
3 jthso103e2w1		<b>MGA</b>	LAG	ADD	C.	AGGT	GCCAG	TCA	GCC	GGAT	CCI	LAAC	CGAT	TT	GACC	GAGA	TCG	GCT	CTTC	AAT	GCC	GTC	T	ccca	3 <b>G</b> G1	ro T	ccc	CGA	GGAT	,
Genbank AA23		CGA	LAG	G:A/	C	AGGT	GCCAG	TCA	GCC	GGA1	CCI	LAAC	CGAT	TT	GACC	GAGA	TCG	GCT	CTTC	AAT	GCC	GTC	T	CCCG	3GG1	TOT	ccc	GA	GGAT	,
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Athmilelire 14			AG	GGA	C	AGGT	GCCA:	TCA	ACC	GGAT	CCI	AAAC	CGAT	TT	GACC	GAGA	TIG	GGT	TTTC	AAT	rc go	GTC	T	ccce	agg:	TOT	ccc	CGA	GGAT	•

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A fibx21611x19_ 4470 CTGGCTGGAC TTCCAGAGTA CCTGAGCAAG ACCAGCAAGT ACCTCACCGN CTCGGAAT: C NCAGAGGG
A firmibilitig. 1470 ctggctggac ttccagagta cctgagcaag accagcaagt acctcaccga ctcggaatac acagagggg
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M K A V L N L K D G V N A C I L P L L Q I D R D 8 G N P O P

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Gembank AA9... $189 GATGGGCTCC TCCAAGCTGG GGCCCGCCTC TGCCCTACCG TGCAGCTTGA GGACATCCGC AACCTGCAGG ATCTCACQ
Gordank AAS. 4189 GATOGOCTCC TCCAAGCTGG GGCCCGCCTC TGCCCTACCG TGCAGCTTGA GGACATCCGC AACCTGCAGG ATCTCACGCC TCTGAAGCTG
                                           CGCCTC TGCCCTACCG TGCAGCTTGA GGACATCCGC AACCTGCAGG ATCTCACGCC TCTGAAGCTG
| jthla029c10t... >#1>
                                             CCTC TGCCCTACCG TGCAGCTTGA GGACATCCGC AACCTGCAGG ATCTCACGCC TCTGAAANTG
@ Genbank W38... >#1>
            #1171 GATGGGCTCC TCCAAGCTGG GGCCCGCCTC TGCCCTACCG TGCAGCTTGA GGACATCCGC AACCTGCAGG ATCTCACGCC TCTGAAGCTG
                   D G L L Q A G A R L C P T V Q L E D I R N L Q D L T P L K L
A frhob12c4g1 .... #321 GCCGCCAAGG AGGGCAAGNT CGANATTTTC AGGCACATCC TGCA
Africado 12:04s... #321 GCCCCCAAGG AGGCCAAGAT CGAGATTTTC AGGCACATCC TGCAGCGGGA GTTTCAGGA CTGAGCCACC TTTCCCGAAA GTTCACCGAG
🔁 friod012c04s... #321 GCCGCCARGG AGGGCAAGAT CGAGATTTTC AGGCACATCC TGCAGCGGGA GTTTTCAGGA CTGAGCCACC TTTCCCGAAA GTTCACCGAG
finoc12c4b3... #313 GCCGCCAAGG AGGGCAAGAT CGAGATTTTC AGGCACATCC TGCAGCGGGA GTTTTCAGGA CTGAGCCACC TTTCCCGAAA GTTCACCGAG
Genbenk AA9... #279 GCCGCCAAGG AGGGCAAGAT CGAGATCTTC AGGCACATCC T
🚧 jtma029c10t1_ 167 GCCGCCAAGO AGGGCAAGAT CGAGATTTTC AGGCACATCC TGCAGCGGGA GTTTCAGGA CTGAGCCACC TTTCCCGAAA GTTCACCOAG
Genbank W186_ $65 GCCGCCAAGG AGGGCAAGAT CGAGATTTC AGGCACATCC TGCAGCGGGA GTTNTCAGGA CTGAGCCACC TTTCCCGAAA GTTCACCGAG
                                                                           TTCAGGA CTGAGCCACC TTTCCCGAAA GTTCACCGAG
Genbank AA3... >#1>
            $1261 GCCGCCAAGG AGGGCAAGAT CGAGATTTTC AGGCACATCC TGCAGCGGGA GTTTTCAGGA CTGAGCCACC TTTCCCGAAA GTTCACCGAG
                                         EIF RHIL QRE FSG LSHL SRK FT E
₹2 fmob012c04s... $411 TGGTGCTATG GGCCTGTCCG GGTGTCGCTG TATGACCTGG CTTCTGTGGA CAGCTGTGAG GAGAACTCAG TGCTGGAGAT CATTGCCTTT
Ethob012c04s... 4411 TGGTGCTATG GGCCTGTCCG GGTGTCGCTG TATGACCT:G CTTCTGTGGA CAGCTGTGAG GAGAACTCAA TGCTGGAGAT CATTGCCTTT
 finocl2c4b3... 4403 Tegtectate egectetee egteteete tateacetee etteteteea cagetetea eagaactea tectegabat cattecett
Sthla029clot. 1157 TGGTGCTATG GGCCTGTCCG GGTGTCGCTG TATGACCTGG CTTCTGTGGA CAGCTGTGAG GAGAACTCAG TGCTGGAGAT CATTGCCTTT
   Genbank W38... 1155 TGGTGCTATG GGCCTGTCCG GGTGTCGCTG TATGACCTGG CTTCTGTGGA CAGCTGTGAG GAGAACTCAG TGCTGGAGAT CATTGCCTTT
   Genbank AA35... $38 TGGTGCTATG GGCCTGTCCG GGTGTCGCTG TATGACCTGG CTTCTNTGGA CAGCTGTNAG GAGAACTCAG TGCTGGAGAT CATTGCCTTT
                             GGCCTGTNCG GGTGTCNCTG TATGACNTGG CTTCTGTGNA CAGCTGTGAN GAGAACTCAG TGCTGGAGAT CATTGCCTTT
frbob12c4c1... >#1>
                                                                                   GAGAACTCAG TGCTGGAGAT CATTGNCTTT
Genbank №4... >41>
             $1351 TGGTGCTATG GGCCTGTCCG GGTGTCGCTG TATGACCTGG CTTCTGTGGA CAGCTGTGAG GAGAACTCAG TGCTGGAGAT CATTGCCTTT
                               PVRVSLYDLASVDSCEENSVLEIIAF
                    WCYG
2 1thob012c04s. 4501 CATTGCAAGA GCCCGCACCG ACACCGAATG GTCGNTTTGG AGCCCCTGAA CAAACTGCTG C
🕰 1:hob012:048... 1501 CATTGCAAGA ACCCGCACCG ACACCGAATG GTCGNTTTGG AGCCCCTGAA CAAACTGCTG CANGCGAAAT GGGATCTGCT CAT:CCCAAG
Ethocl2c4h3... 1493 CATTGCAAGA GCCCGCACCG ACACCGAATG GTCGTTTTGH AGCCCCTGAA CAAACTGCTG CAGGCGAAAT GGGATCTGCT CATCCCCAA
🔁 jibla029c10t... 1247 - Cattgcaaga Gcccgnaccg acaccgaatg Gtcgttttgg agcccctgaa Caaactgctg Cangcgaaat Gggatctgct Catncncaag
Goddank M38. 1245 Cattgcaaga gcccgcaccg acaccgaatg gtcgttttgg agcccctgaa caaactgctg caggcgaaat gggatctgct catccccaag
   Genbank AA3. #128 CATTGCAAGA GCCCGCACCG ACACCGAATG GTCGTTTTGG AGCCCCTGAA CAAACTGCTG CAGGCGAAAT GGGATCTGCT CATCCCCAAG
€ Ethob12c4c1.a... 481 CATTGCAAGA GECCGCACCG ACACHGAATG GTCGTTTTGG AGCCCCTGAA CAAACTGCTG CAGNCGAAAT GGGATCTGCT CATCCCCAAG
   Genbank N242... #31 CATTGCAAGA GCCCGNACCG ACACCGAATG GTCGTTTTGG AGCCCCTGAA CAAACTGCTG CAGGCGAAAT GGGATCTGCT CATCCCCAAG
             $1441 CATTGCAAGA GCCCGCACCG ACACCGAATG GTCGTTTTGG AGCCCCTGAA CAAACTGCTG CAGGCGAAAT GGGATCTGCT CATCCCCAAG
                    R C K S P H R H R M V V L B P L N K L L Q A K W D L L I P K
```

Achrh21e11 #425 frtob12c4d1 >#1>	GGCACTAA	GC C/	AGATGG	CAG	ccca	GATGAG	CGC1	rggt	GCT	TCAGO	GTGGA	GGA	GTGAA	C TG	GGC1				CAGAG			
#2431	GGCACTAA				CCCG	IGATGAG D B	CGCT R		GCT C I		KODTOGA V E		aadtde n v		GGC:	-	T G	ggag E		GCT L	3CC1	'ACG T
Achyrb21e11 #515 2 frhob12c4d1.a #25																						
#2521	CTGTGTGA L C E		CCCGTC			G V		CGAA R					CCTGGC L A			TCCC P			D I			
Achrh21e11 \$605																						
<b>\$2611</b>	TCTGAGGA S E B		CTATG1		CGTC V	CAGCTC Q L	CTC		CCA S 1		ATGGCC W 1		ATGCAG C S		GAG R		G A		R A			
Achrh21e11 #695																						LAAA
<b>\$2701</b>	TCCAACCA S N H					G P			rtct F		Q S		TATTTI I F			CTCA S			AAAA K 3			
<b>2</b> frhob12c4d1 #295	AAAAAAA	AA A	AAAAA	AAA																		
#2791	AAAAAAA K K R																					

```
BLASTP vs. PNU (AA) flh21ellorfaa - 5:26:57 pm on Dec 21 98
BLASTP 1.4.10MP-WashU [30-Aug-96] (Build 20:24:58 Oct 21 1996]
Reference: Altschul, Stephen F., Warren Gish, Webb Miller, Eugene W. Myers,
and David J. Lipman (1990). Basic local alignment search tool. J. Mol. Biol.
215:403-10.
Query= flh21e11orfaa
        (764 letters)
           /disk0/asap/databases/db/NRP/protxnu
           345,099 sequences; 106,000,184 total letters.
Searching......done
                                                                    Smallest
                                                                       Sum
                                                             High
                                                                   Probability
Sequences producing High-scoring Segment Pairs:
                                                            Score
                                                                   P(N)
                                                                   1,9e-221
GP:gi|2570933 (AF029310) vanilloid receptor subtype 1 [Ra...
                                                               336
                                                                             7
GPU:gi | 3986159 | gpl | PID | d1035925 (AB015231) VR1sk [Mus mus...
                                                                   9.8e-136
                                                                             6
                                                               299
GP:gi 2911863 (AF047660) contains similarity to ankyrin r...
                                                               103
                                                                   6.5e-20
                                                                              R
GP:gi|3675319|gml|PID|e1344970 (Z74030) similar to ankyri...
                                                                              7
                                                               97
                                                                   1.1e-19
GP:gi 2642590 (AF031408) olfactory channel [Caenorhabditi...
                                                               93
                                                                   3.6e-16
                                                                              6
GP:gi 2854148 (AF045639) contains similarity to ankyrin r...
                                                                93
                                                                  4.1e-16
GP:gi 3879753 gnl PID e1349345 (Z72514) Similarity to Hum...
                                                                   3.6e-11
                                                                73
GP:gi 3287188 gml PID e315126 (Y10601) ankyrin-like prote...
                                                                71
                                                                   2.7e-08
SP:SP:SP P48994 TRPL_DROME TRANSIENT-RECEPTOR-POTENTIAL L...
                                                                69
                                                                   2.2e-05
                                                                              4
                                                                72
                                                                   5.6e-05
GP:gi | 1841966 (U65916) ankyrin [Rattus norvegicus]
          Descriptions of 4 database sequences were not reported due to the
WARNING:
          limiting value of parameter V = 10^{\circ}.
>GP:gi|2570933 (AF029310) vanilloid receptor subtype 1 [Rattus norvegicus]
            Length = 838
 Score = 336 (156.0 bits), Expect = 1.9e-221, Sum P(7) = 1.9e-221
 Identities = 67/112 (59%), Positives = 84/112 (75%)
         206 FYFGELPLSLAACTKQWDVVSYLLENPHQPASLQATDSQGNTVLHALVMISDNSAENIAL 265
Query:
             FYFGELPLSLAACT Q +V +LL+N QPA + A DS GNTVLHALV ++DN+ +N
         245 FYFGELPLSLAACTNQLAIVKFLLQNSWQPADISARDSVGNTVLHALVEVADNTVDNTKF 304
Sbjct:
         266 VTSMYDGLLQAGARLCPTVQLEDIRNLQDLTPLKLAAKEGKIEIFRHILQRE 317
Query:
             VTSMY+ +L GA+L PT++LE+1 N + LTPL LAA GKI + +ILQRE
         305 VTSMYNEILILGAKLHPTLKLEEITNRKGLTPLALAASSGKIGVLAYILQRE 356
Sbjct:
 Score = 316 (146.7 bits), Expect = 1.9e-22\%. Sum P(7) = 1.9e-22\%
 Identities = 65/138 (47%), Positives = 93/138 (67%)
          66 ASQPDPNRFDRDRLFNAVSRGVPEDLAGLPEYLSKTSKYLTDSEYTEGSTGKTCLMKAVL 125
Query:
                                   ++L L +L ++ K LTDSE+ + TGKTCL+KA+L
             A + P +DR +F+AV++
         104 AGEKPPRLYDRRSIFDAVAQSNCQELESLL!FLQRSKKRLTDSEFKDPETGKTCLLKAML 163
Sbjct:
         126 NLKDGVNACILPLLQIDRDSGNPQPLVNAQCTDDYYRGHSALHIAIEKRSLQCVKLLVEN 185
Query:
             NL +G N I LL + R + + + VNA TD YY+G +ALHIAIE+R++ | V LLVEN
         164 NLHNGQNDTIALLLDVARKTDSLKQFVNAS!TDSYYKGQTALHIAIERRNMTLVTLLVEN 223
Sbjct:
         186 GANVHARACGRFFQKGQG 203
Query:
```

GA+V A A G FF+K +G

Sbjct: 224 GADVQAAANGDFFKKTKG 241

Score = 299 (138.8 bits), Expect = 1.9e-221, Sum P(7) = 1.9e-221 Identities = 69/175 (39%), Positives = 94/175 (53%)

Query: 391 FFLNFLCNLIYMFIFTAVAYHQPTLKKAAPHLKAEVGNSMLLTGHILILLGGTYLLVGQL 450 F+ NF +YM IFTA AY++P LK VG+ +TG IL + +

F+ NF +YM IFTA AY++P LK VG+ +TG IL + +
Sbjct: 434 FYFNFFVYCLYMIIFTAAAYYRPVEGLPPYKLKNTVGDYFRVTGEILSVXXXXXXXRGI 493

Query: 451 WYFWRRHVFIWISFIDSYFEILFLFQALLKPVSQVLCFLAIEWYLPLLVSALPLGWLNLL 510

YF +R + F+DSY EILF Q+L VS VL F + Y+ +V +L +GW N+L Sbjct: 494 QYFLQRRPSLKSLFVDSYSEILFFVQSLF1:LVSVVLYFSQRKEYVASMVFSLAMGWTNML 553

Query: 511 YYTRGFQHTGIYSVMIQKVILRDLLRFLLTYLVFLFGFAVALVSLSQEAWRPEAP 565
YYTRGFQ GIY+VMI+K+ILRDL R A+V+L ++ P

Sbjct: 554 YYTRGFQQMGIYAVMIEKMILRDLCRXXXXXXXXXXXXXXXXXXTAVVTLIEDGKNNSLP 608

Score = 281 (130.5 bits), Expect = 1.9e-221, Sum P(7) = 1.9e-221 Identities = 54/95 (56%), Positives = 70/95 (73%)

Query: 586 GAQYRGILEASLELFKFTIGMGELAFQEQLHFRGMVLLLLLAYVLLTYILLLNMLIALMS 645

G Y + LELFKFTIGMG+L F E F+ + ++LLLAYV+LTYILLLNMLIALM

Sbjct: 624 GNSYNSLYSTCLELFKFTIGMGDLEFTENYDFKAVFIILLLAYVILTYILLLNMLIALMG 683

Query: 646 ETVNSVATDSWSIWKLQKAISVLEMENGYWWCRKK 680

ETVN +A +S +IWKLQ+AI++L+ E + C +K

Sbjct: 684 ETVNKIAQESKNIWKLQRAITILDTEKSFLKCMRK 718

Score = 162 (75.2 bits), Expect = 1.9e-221, Sum P(7) = 1.9e-221 Identities = 28/38 (73%), Positives = 34/33 (89%)

Query: 323 HLSRKFTEWCYGPVRVSLYDLASVDSCEENSVLEIIAF 360

HLSRKFTEW YGPV SLYDL+ +D+CE+NSVLE+IA+

Sbjct: 364 HLSRKFTEWAYGPVHSSLYDLSCIDTCEKNSVLEVIAY 401

Score = 144 (66.9 bits), Expect = 1.9e-221, Sum P(7) = 1.9e-221 Identities = 25/47 (53%), Positives = 31/47 (65%)

Query: 678 RKKORAGVMLTVGTKPDGSPDERWCFRVEEVNWASWEOTLPTLCEDP 724

RK R+G +L VG PDG D RWCFRV+EVNW +W + + EDP

Sbjct: 717 RKAFRSGKLLQVGFTPDGKDDYRWCFRVDEVNWTTWNTNVGIINEDP 763

Score = 94 (43.6 bits), Expect = 1.9e-221, Sum P(7) = 1.9e-221 Identities = 15/30 (50%), Positives = 24/30 (80%)

Query: 363 KSPHRHRMVVLEPLNKLLQAKWDLLIPKFF 392

++P+RH M+++EPLN+LLQ KWD + + F

Sbjct: 405 ETPNRHDMLLVEPLNRLLQDKWDRFVKRIF 434

Score = 46 (21.4 bits), Expect = 1.3e-162 Sum P(6) = 1.3e-162 Identities = 11/48 (22%), Positives = 24/43 (50%)

Query: 435 HILILLGGIYLLVGQLWYFWRRHVFIWISFIDSYFEILFLFQALLKPV 482

H ++L+ + L+ W + + +F + F+ + I+F A +PV Sbjct: 410 HDMLLVEPLNRLLQDKWDRFVKRIFYFNFFVYCLYMIIFTAAAYYRPV 457

Score = 37 (17.2 bits), Expect = 2.4e-169, Sum P(7) = 2.4e-169 Identities = 8/22 (36%), Positives = 13/22 (59%)

Query: 297 PLKLAAKEGKIEIFRHILQREF 318

PL LAA ++ I + +LQ +

Sbjct: 251 PLSLAACTNQLAIVKFLLQNSW 272

Score = 37 (17.2 bits), Expect = 1.9e-111, Sum P(7) = 1.9e-111Identities = 8/26 (30%), Positives = 15/26 (57%) 206 FYFGELPLSLAACTKQWDVVSYLLEN 231 Query: +Y G+ L +A + +V+ L+EN 198 YYKGOTALHIAIERRNMTLVTLLVEN 223 Sbjct: >GPU:gi|3986159|gnl|PID|d1035925 (AB015231) VRlsk [Mus musculus] Length = 563Score = 299 (138.8 bits), Expect = 9.8e-136, Sum P(6) = 9.8e-136Identities = 69/175 (39%), Positives = 94/175 (53%) 391 FFLNFLCNLIYMFIFTAVAYHQPTLKKAAPHLKAEVGNSMLLTGHILILLGGIYLLVGQL 450 +TG IL + +YM IFTA AY++P LK VG+ F+ NF 127 FYFNFFVYCLYMIIFTAAAYYRPVEGLPPYKLKNTVGDYFRVTGEILSVXXXXXXXRGI 186 Sbjct: 451 WYFWRRHVFIWISFIDSYFEILFLFQALLKPVSQVLCFLAIEWYLPLLVSALVLGWLNLL 510 Query: VS VL F + Y+ +V +L +GW N+L F+DSY EILF Q+L + 187 QYFLQRRPSLKSLFVDSYSEILFFVQSLFMLVSVVLYFSQRKEYVASMVFSLAMGWTNML 246 Sbjct: 511 YYTRGFQHTGIYSVMIQKVILRDLLRFLLIYLVFLFGFAVALVSLSQEAWRPEAP 565 Query: YYTRGFO GIY+VMI+K+ILRDL R A+V+L ++ 247 YYTRGFQQMGIYAVMIEKMILRDLCRXXXXXXXXXXXXXXXTAVVTLIEDGKNNSLP 301 Sbjct: Score = 253 (117.5 bits), Expect = 9.8e-136, Sum P(6) = 9.8e-136 Identities = 50/89 (56%), Positives = 64/89 (71%) 586 GAQYRGILEASLELFKFTIGMGELAFQEQLHFRGMVLLLLLAYVLLTYILLLNMLIALMS 645 Ouerv: LELFKFTIGMG+L F E F+ + ++LLLAYV+LTYILLLNMLIALM 317 GNSYNSLYSTCLELFKFTIGMGDLEFTENYDFKAVFIILLLAYVILTYILLLNMLIALMG 376 Sbjct: 646 ETVNSVATDSWSIWKLQKAISVLEMENGY 674 Query: ETV V+ +S IWKLQ A ++L++E + 377 ETVGQVSKESKHIWKLQWATTILDIERSF 405 Sbjet: Score = 163 (75.7 bits), Expect = 9.8e-136, Sum P(6) = 9.8e-136Identities = 28/47 (59%), Positives = 34/47 (72%) 678 RKKQRAGVMLTVGTKPDGSPDERWCFRVEEVNWASWEQTLPTLCEDP 724 Query: RK R+G M+TVG DG+PD RWCFRV+EVNW+ W Q L + EDP 410 RKAFRSGEMVTVGKSSDGTPDRRWCFRVDEVNWSHWNQNLGIINEDP 456 Sbjct: Score = 162 (75.2 bits), Expect = 9.8e-136, Sum P(6) = 9.8e-136Identities = 28/38 (73%), Positives = 34/3 (89%) Query: 323 HLSRKFTEWCYGPVRVSLYDLASVDSCEENSVLEIIAF 360 HLSRKFTEW YGPV SLYDL+ +D+CE+NSVLE+LA+ 57 HLSRKFTEWAYGPVHSSLYDLSCIDTCEKNSVLEVIAY 94 Sbict: Score = 129 (59.9 bits), Expect = 9.8e-136, Sum P(6) = 9.8e-136Identities = 27/49 (55%), Positives = 36/49 (73%) 269 MYDGLLQAGARLCPTVQLEDIRNLQDLTPLKLAAKEGKIEIFRHILQRE 317 Query: MY+ +L GA+L PT++LE+I N + LTPL LAA GKI + +ILQRE 1 MYNEILILGAKLHPTLKLEEITNRKGLTPLALAASSGKIGVLAYILQRE 49 Sbjct:

Score = 94 (43.6 bits), Expect = 9.8e-136, Sum P(6) = 9.8e-136

[Identities = 15/30 (50%), Positives = 24/30 (80%)

Query: 363 KSPHRHRMVVLEPLNKLLQAKWDLLIPKFF 392

++P+RH M+++EPLN+LLQ KWD + + F

98 ETPNRHDMLLVEPLNRLLQDKWDRFVKRIF 127 Sbjct:

Score = 46 (21.4 bits), Expect = 2.3e-77, Sum P(5) = 2.3e-77Identities = 11/48 (22%), Positives = 24/48 (50%)

435 HILILLGGIYLLVGQLWYFWRRHVFIWISFIDSYFEILFLFQALLKPV 482 Ouerv: H ++L+ + L+ W + + +F + F+ + I+F A +PV

103 HDMLLVEPLNRLLQDKWDRFVKRIFYFNFFVYCLYMIIFTAAAYYRPV 150 Sbjct:

Score = 42 (19.5 bits), Expect = 1.2e-122, Sum P(6) = 1.2e-122Identities = 9/22 (40%), Positives = 16/22 (72%)

209 GELPLSLAACTKQWDVVSYLLE 230 G PL+LAA + + V++Y+L+ 26 GLTPLALAASSGKIGVLAYILQ 47 Sbjct:

Sbjct:

>GP:gi 2911863 (AF047660) contains similarity to ankyrin repeats [Caenorhabditis elegans] Length = 900

Score = 103 (47.8 bits), Expect = 6.5e-20, Sum P(8) = 6.5e-20Identities = 23/89 (25%), Positives = 44/39 (49%)

497 LLVSALVLGWLNLLYYTRGFQHTGIYSVMIQKVILRDLLRFLLIYLVFLFGFAVALVSLS 556 Query: ++ ++ LYY R + G + +M+ +I D+ RF+LIY +FL GF+ + 592 LITVTMIFTTVHYLYYCRVIRFVGPFVLMVYTIIATDIFRFMLIYGIFLMGFSQSFSLIF 651

557 QEAWRPEAPTGPNATESVQPMEGQEDEGN 585 Ouery: T+ + EG +++ N R

652 LSCEREANVIKKLITDQSEASEGSDNKFN 680 Sbjct:

Score = 63 (29.3 bits), Expect = 6.5e-20, Sum P(8) = 6.5e-20 Identities = 15/27 (55%), Positives = 18/27 (66%)

291 NLQDLTPLKLAAKEGKIEIFRHILQRE 317 Query: N Q L+PL LAAK K E+F IL+ E 328 NKQSLSPLTLAAKLAKKEMFDEILELE 354 Sbjct:

Score = 56 (26.0 bits), Expect = 6.5e-20, Sum P(8) = 6.5e-20Identities = 16/48 (33%), Positives = 25/48 (52%)

151 LVNAQCTDDYYRGHSALHIAIEKRSLQCVKLLVENGANVHARACGRFF 198 Query: + V ++ GA+V++R G FF + + G S LH AI L+N185 LLNDIHISEDFYGLSPLHQAIINTDCKLVYKFLKLGADVNSRCYGAFF 232 Sbjct:

Score = 54 (25.1 bits), Expect = 6.5e-20, Sum P(8) = 6.5e-20Identities = 12/23 (52%), Positives = 13/23 (56%)

207 YFGELPLSLAACTKQWDVVSYLL 229 Query: Y GE PLS AAC Q + 263 YLGEYPLSFAACLNQPESFRLLL 285 Sbjct:

Score = 49 (22.8 bits), Expect = 6.5e-20, Sum P(8) = 6.5e-20Identities = 8/23 (34%), Positives = 12/23 (52%)

331 WCYGPVRVSLYDLASVDSCEENS 353 Query: + Y LA +D+ E + W YG 359 WAYGDASSTAYPLAKIDTINETT 381 Sbjct:

Score = 47 (21.8 bits), Expect = 6.5e-20,  $\operatorname{Sum} P(8) = 6.5e-20$ Identities = 11/30 (36%), Positives = 18/30 (60%)

Query: 236 ASLQATDSQGNTVLHALVMISDNSAENIAL 265
A+ A D+ GN+VLH V+ + + +AL

Sbjct: 289 ANPNAQDTNGNSVLHMCVIHENMAMFKLAL 318

Score = 46 (21.4 bits), Expect = 5.7e-13, Sum P(6) = 5.7e-13Identities = 9/27 (33%), Positives = 17/27 (62%)

Query: 163 GHSALHIAIEKRSLQCVKLLVENGANV 189
G+S LH+ + ++ KL +E GA++
Sbjct: 298 GNSVLHMCVIHENMAMFKLALECGASL 324

Score = 43 (20.0 bits), Expect = 6.5e-20, Sum P(8) = 6.5e-20 Identities = 8/18 (44%), Positives = 13/18 (72%)

Query: 634 ILLINMLIALMSETVNSV 651 I+ NMLIA+M+ T ++

Sbjct: 753 IMQFNMLIAMMTRTYETI 770

Score = 41 (19.0 bits), Expect = 6.5e-20, Sum P(8) = 6.5e-20 Identities = 10/27 (37%), Positives = 16/27 (59%)

Query: 113 GSTGKTCLMKAVLNLKDGVNACILFLL 139
GS G+T + +L+ D NA +L +L
Sbjct: 153 GSMGETIIGCCLLHASDIHNALVLKIL 179

Score = 35 (16.3 bits), Expect = 0.00016, Sum P(3) = 0.00016 Identities = 9/37 (24%), Positives = 16/37 (43%)

Query: 67 SOPDPNRFDRDRLFNAVSRGVPEDLAGLPEYLSKTSK 103 S+P P R+ ++ V + GL E+ S+ Sbjct: 464 SEPFPGRYGKNSTLQQVKPVINATSRGLVEWSEPLSQ 500

Score = 34 (15.8 bits), Expect = 6.8e-11, Sum P(8) = 6.8e-11 Identities = 8/31 (25%), Positives = 17/31 (54%)

Query: 422 LKAEVGNSMLLTGHILLLGGIYLLVGQLWY 452 L ++ +L+ ++LI + I+ V L+Y Sbjct: 577 LACDLSPVLLVVDNVLITVTMIFTTVHYLYY 607

>GP:gi|3875319|gnl|FID|e1344970 (Z74030) similar to ankyrin repeats
[Caenorhabditis elegans] >GP:gi|3876480|gnl|FID|e1346172 (Z72508)
similar to ankyrin repeats [Caenorhabditis elegans]
Length = 790

Score = 97 (45.0 bits), Expect = 1.1e-19, Sum P(7) = 1.1e-19 Identities = 18/53 (33%), Positives = 32/53 (60%)

Query: 497 LLVSALVLGWLNLLYYTRGFQHTGIYSVMIQKVILRDLLRFLLIYLVFLFGFA + + ++++ + LYY R G + +m+ +I DL+RF +IY +FL GF+ Sbjct: 526 MAIISILLVTQHFLYYMRAIPFVGPFVLMVYTIIATDLVRFAMIYSIFLVGFS 578

Score = 89 (41.3 bits), Expect = 1.1e-19, Sum P(7) = 1.1e-19 Identities = 19/48 (39%), Positives = 27/48 (56%)

Query: 151 LVNAQCTDDYYRGHSALHIAIEKRSLQCVKLLVENGANVHARACGRFF 198 L+N C + Y G S LH+AY + Q LL+ GA+++ R G FF Sbjct: 189 LINDICVSEEYYGLSPLHLAIVNQDAQFTSLLLRLGADLNQRCYGAFF 236

Score = 62 (28.8 bits), Expect = 1.1e-19, Sum P(7) = 1.1e-19 Identities = 13/23 (56%), Positives = 14/23 (60%)

Query: 207 YFGELPLSLAACTKQWDVVSYLL 229

YFGE PLS A C Q D+ LL

Sbjct: 267 YFGEYPLSFAICMGQHDLFRMLL 289

Score = 51 (23.7 bits), Expect = 1.1e-19, Sum P(7) = 1.1e-19

Identities = 10/19 (52%), Positives = 13/19 (68%)

Query: 236 ASLQATDSQGNTVLHALVM 254

A+L A D+ GNT LH V+

Sbjct: 293 ANLSAQDTNGNTALHLCVI 311

Score = 49 (22.8 bits), Expect = 1.1e-19, Sum P(7) = 1.1e-19

Identities = 11/51 (21%), Positives = 27/51 (52%)

Query: 601 KFTIGMGELAFQEQLHFRGMVLLLLLAYVLLTYILLINMLIALMSETVNSV 651

+F++ E++ + + + L+ + IL N+LIA+M+ T ++

Sbjct: 626 EFSVLYREMSACDNFWMKWIGKLIFVIFET: SILQFNLLIAMMTRTYETI 676

Score = 43 (20.0 bits), Expect = 1.2e-06, Sum P(5) = 1.2e-06

Identities = 7/27 (25%), Positives = 16/27 (59%)

Query: 163 GHSALHIAIEKRSLQCVKLLVENGANV 189

G++ALH+ + + + ++E G N+

Sbjct: 302 GNTALHLCVIHDKMDMLDAVLEAGGNI 328

Score = 39 (18.1 bits), Expect = 5.5e-12, Sum P(7) = 5.5e-12

Identities = 12/56 (21%), Positives = 25/56 (44%)

Query: 461 WISFIDSYFEILFLFQALLKPVSQVLCFLAIEWYLPLLVSALVLGWLNLLYYTRGF 516

W +F+ ++ L AL + + C LA ++ L + +++L T + F

Sbjct: 483 WFNFLKAFPAKLMFKGAFLFIIISIPCRLACSFHEFFLTIDNTMAIISILLVTOHF 538

Score = 38 (17.6 bits), Expect = 1.1e-19, Sum P(7) = 1.1e-19 Identities = 9/18 (50%), Positives = 12/18 (66%)

Identifica - by to (Book) Tobicatob - 11/1

289 IRNLQDLTPLKLAAKEGK 306

+ N Q+LT L LAA+ K Sbjct: 330 LANKQNLTALTLAARLAK 347

Score = 37 (17.2 bits), Expect = 4.7e-18, Sum P(7) = 4.7e-18

Identities = 7/15 (46%), Positives = 9/15 (60%)

Query: 723 DPSGAGVPRTLENPV 737

Ouerv:

DP G+ +ENPV

Sbjct: 599 DPMGSEFNNIMENPV 613

Score = 36 (16.7 bits), Expect = 1.1e-19, Sum P(7) = 1.1e-19

Identities = 10/47 (21%), Positives = 16/47 (34%)

Query: 376 LNKLLQAKWDLLIPKFFLNFLCNLIYMFIFTAVAYHQPTLKKAAPHL 422

+ ++L KW +L L I+ + AY HL

Sbjct: 362 IEQILDEKWKAYGRALWLRSLLGFIFFYCCFVCAYMLRPSSATTEHL 408

Score = 35 (16.3 bits), Expect = 3.0e-08, 90m P(6) = 3.0e-08

Identities = 9/23 (39%), Positives = 11/23 (47%)

Query: 207 YFGELPLSLAACTKQWDVVSYLL 229

Y+G PL LA + S LL

Sbjct: 199 YYGLSPLHLAIVNQDAQFTSLLL 221

Score = 34 (15.8 bits), Expect = 3.9e-12, Sum P(5) = 3.9e-12

Identities = 7/21 (33%), Positives = 13/21 (61%)

Query: 297 PLKLAAKEGKIEIFRHILQRE 317

PL A G+ ++FR +L ++

Sbjct: 272 PLSFAICMGQHDLFRMLLAKK 292

Score = 34 (15.8 bits), Expect = 8.9e-10, Sum P(7) = 8.9e-10

Identities = 6/18 (33%), Positives = 12/18 (66%)

Query: 610 AFQEQLHFRGMVLLLLLA 627

AF +L F+G L ++++

Sbjct: 489 AFPAKLMFKGAFLFIIIS 506

Score = 34 (15.8 bits), Expect = 4.0e-08, Sum P(6) = 4.0e-08

Identities = 11/40 (27%), Positives = 16/40 (40%)

Query: 153 NAQCTDDYYRGHSALHIAIEKRSLQCVKLLVENGANVHAR 192

N T YG L AI ++L+ AN+ A+

Sbjcc: 259 NTNYTGSMYFGEYPLSFAICMGQHDLFRMLLAKKANLSAQ 298

>GP:gi 2642590 (AF031408) olfactory channel [Caenorhabditis elegans] Length = 937

Score = 93 (43.2 bits), Expect = 6.8e-16, Sum P(5) = 6.8e-16 Identities = 19/36 (52%), Positives = 25/36 (69%)

Query: 163 GHSALHIAIEKRSLQCVKLLVENGANVHARACGRFF 198

G SALH+AI + V LL+ + A+V+ARACG FF

Sbjct: 172 GQSALHLAIVHDDYETVSLLLNSKADVNARACGNFF 207

Score = 92 (42.7 bits), Expect = 6.8e-16, Sum P(5) = 6.8e-16

Identities = 20/53 (37%), Positives = 31/53 (58%)

Query: 497 LLVSALVLGWLNLLYYTRGFQHTGIYSVMIQKVILRDLLRFLLIYLVFLFGFA 549

L V AL W+ LL++ R + TG + MI +I D++RF +I +FL F+

Sbjct: 500 Lfvfalpgswifllffarsakltgpfvqmiysmiagdmirfaiisaiflvsfs 552

Score = 57 (26.5 bits), Expect = 6.8e-16, Sum P(5) = 6.8e-16 Identities = 10/24 (41%), Positives = 15/24 (62%)

Y+GE PL+ AAC D+ L++

207 YFGELPLSLAACTKQWDVVSYLLE 230

Sbjct: 226 YYGEYPLAFAACFGNKDIYDLLIQ 249

Query:

Score = 50 (23.2 bits), Expect = 6.8e-16, Sum P(5) = 6.8e-16

Identities = 11/25 (44%), Positives = 15/25 (60%)

Query: 291 NLQDLTPLKLAAKEGKIEIFRHILQ 315

N TPL LAKG+ +IF +L+

Sbjct: 294 NHAGFTPLTLATKLGRKQIFEEMLE 318

Score = 44 (20.4 bits), Expect = 6.8e-16, Sam P(5) = 6.8e-16

Identities = 10/24 (41%), Positives = 15/24 (62%)

Query: 242 DSQGNTVLHALVMISDNSAENIAL 265

DS GNT+LH V+ +S + A+

Sbjct: 258 DSFGNTILHMCVINYSSSMYSYAV 281

Score = 37 (17.2 bits), Expect = 2.2e-05, Sum P(4) = 2.2e-05

Identities = 9/24 (37%), Positives = 13/24 (54%)

Query: 208 FGELPLSLAACTKQWDVVSYLLEN 231

FG+ L LA ++ VS LL +

Sbjct: 171 FGQSALHLAIVHDDYETVSLLLNS 194

Score = 34 (15.8 bits), Expect = 3.6e-16, Sum P(6) = 3.6e-16Identities = 7/21 (33%), Positives = 11/21 (52%)

Query: 364 SPHRHRMVVLEPLNKLLQAKW 384 +P M+ E + +LL KW Sbjct: 363 TPEHLDMIGSEVIQRLLADKW 383

>GP:gi|2854148 (AF045639) contains similarity to ankyrin repeats [Caenorhabditis elegans]
Length = 957

Score = 93 (43.2 bits), Expect = 7.6e-16, Sum F(5) = 7.6e-16Identities = 19/36 (52%), Positives = 25/36 (69%)

Query: 163 GHSALHIAIEKRSLQCVKLLVENGANVHARACGRFF 198
G SALH+AI + V LL+ + A+V+ARACG FF
Sbjct: 175 GQSALHLAIVHDDYETVSLLLNSKADVNARACGNFF 210

Score = 92 (42.7 bits), Expect = 7.6e-16, Sum P(5) = 7.6e-16Identities = 20/53 (37%), Positives = 31/53 (58%)

Query: 497 LLVSALVLGWLNLLYYTRGFQHTGIYSVMIQKVILRDLLRFLLIYLVFLFGFA 549
L V AL W+ LL++ R + TG + MI +I D++RF +I +FL F+
Sbjct: 503 LFVFALPGSWIFLLFFARSAKLTGPFVQMIYSMIAGDMIRFAIISAIFLVSFS 555

Score = 57 (26.5 bits), Expect = 7.6e-16, Sum P(5) = 7.6e-16 Identities = 10/24 (41%), Positives = 15/24 (62%)

Query: 207 YFGELPLSLAACTKQWDVVSYLLE 230 Y+GE PL+ AAC D+ L++ Sbjct: 229 YYGEYPLAFAACFGNKDIXDLLIQ 252

Score = 50 (23.2 bits), Expect = 7.6e-16, Sum F(5) = 7.6e-16 Identities = 11/25 (44%), Positives = 15/25 (60%)

Query: 291 NLQDLTPLKLAAKEGKIEIFRHILQ 315 N TPL LA K G+ +IF +L+ Sbjct: 297 NHAGFTPLTLATKLGRKQIFEEMLE 321

Score = 44 (20.4 bits), Expect = 7.6e-16, Sum P(5) = 7.6e-16 Identities = 10/24 (41%), Positives = 15/24 (62%)

Query: 242 DSQGNTVLHALVMISDNSAENIAL 265 DS GNT+LH V+ +S + A+ Sbjct: 261 DSFGNTILHMCVINYSSSMYSYAV 284

Score = 37 (17.2 bits), Expect = 2.4e-05, Sum P(4) = 2.4e-05Identities = 9/24 (37%), Positives = 13/24 (54%)

Query: 208 FGELPLSLAACTKQWDVVSYLLEN 231
FG+ L LA ++ VS LL +
Sbjct: 174 FGQSALHLAIVHDDYETVSLLINS 197

Score = 34 (15.8 bits), Expect = 4.1e-16, Sum P(6) = 4.1e-16 Identities = 7/21 (33%), Positives = 11/21 (52%)

Query: 364 SPHRHRMVVLEPLNKLLQAKW 384 +P M+ E + +LL KW Sbjct: 366 TPEHLDMIGSEVIQRLLADKW 386 >GP:gi|3879753|gn1|PID|e1349345 (Z72514) Similarity to Human ankyrin (SW:ANK1\_HUMAN) [Caenorhabditis elegans]
Length = 519

Score = 73 (33.9 bits), Expect = 3.6e-11, Sum P(6) = 3.6e-11 Identities = 17/36 (47%), Positives = 19/36 (52%)

Query: 163 GHSALHIAIEKRSLQCVKLLVENGANVHARACGRFF 198 G S LH AI L+ V L GA+VH R G FF Sbjct: 186 GLSPLHQAIVNEDLEMVYFLCRKGADVHQRCYGSFF 221

Score = 63 (29.3 bits), Expect = 3.6e-11, Sum P(6)  $\approx$  3.6e-11 Identities = 12/17 (70%), Positives  $\approx$  13/17 (76%)

Query: 207 YFGELPLSLAACTKQWD 223 Y+GE PLS AACT Q D Sbjct: 252 YWGEYPLSFAACTNQVD 268

Score = 52 (24.1 bits), Expect = 3.6e-11, Sum P(6) = 3.6e-11Identities = 13/27 (40%), Positives = 17/27 (62%)

Query: 289 IRNLQDLTPLKLAAKEGKIEIFRHILQ 315 +RN LTPL LAA+ K I+ IL+ Sbjct: 315 VRNNLKLTPLALAARLAKKHIYDLILE 341

Score = 51 (23.7 bits), Expect = 3.6e-11, Sum P(6) = 3.6e-11 Identities = 10/22 (45%), Positives = 12/22 (54%)

Query: 331 WCYGPVRVSLYDLASVDSCEEN 352 W YGPV Y L VD+ E+ Sbjct: 348 WRYGPVVCKAYPLNDVDTINES 369

Score = 43 (20.0 bits), Expect = 3.6e-11, Sum P(6) = 3.6e-11 Identities = 8/13 (61%), Positives = 10/13 (76%)

Query: 242 DSQGNTVLHALVM 254 D+ GNTVLH V+ Sbjct: 284 DTNGNTVLHLTVI 296

Score = 37 (17.2 bits), Expect = 3.6e-11, Sum P(6) = 3.6e-11 Identities = 8/35 (22%), Positives = 16/35 (45%)

Query: 376 LNKLLQAKWDLLIPKFFLNFLCNLIYMFIF®3VAY 410 + ++L++KW+ K L IY +A+ Sbjct: 398 IEEVLESKWETFGKKQLFMSLAGYIYFLAVFYLAF 432

>GP:gi|3287188|gml|PID|e315126 (Y10601) ankyrin-like protein [Homo sapiens]
Length = 1119

Score = 71 (33.0 bits), Expect = 2.7e-08, Sum P(6) = 2.7e-08 Identities = 13/30 (43%), Positives = 20/30 (66%)

Query: 163 GHSALHIAIEKRSLQCVKLLVENGANVHAR 192 G++ LH A+EK ++ VK L+ GAN + R Sbjct: 98 GNTPLHCAVEKNQIESVKFLLSRGANPNLR 127

Score = 63 (29.3 bits), Expect = 2.7e-08, Sum P(6) = 2.7e-08Identities = 10/30 (33%), Positives = 20/30 (66%)

Query: 501 ALVLGWLNLLYYTRGFQHTGIYSVMIQKVI 530 A+ W+N L Y + F++ GI+ VM++ ++ Sbjct: 838 AVYFYWMNFLLYLQRFENCGIFIVMLEVIL 467 Score = 59 (27.4 bits), Expect = 9.0e-07, Som P(6) = 9.0e-07 Identities = 10/30 (33%), Positives = 19/30 (63%)

Query: 167 LHIAIEKRSLQCVKLLVENGANVHARACGR 196 LH+A++ L+ +K+ ++NGA + GR Sbjct: 243 LHLAVQNGDLEMIKMCLDNGAQIDPVEKGR 272

Score = 50 (23.2 bits), Expect = 2.7e-08, Sum P(6) = 2.7e-08Identities = 10/26 (38%), Positives = 18/26 (69%)

Query: 291 NLQDLTFLKLAAKEGKIEIFRHILQR 316 +L +TPL LAAK G ++ + +L++ Sbjct: 479 DLHGMTPLHLAAKNGHDKVVQLLLKK 504

Score = 49 (22.8 bits), Expect = 2.7e-08, Sum P(6) = 2.7e-08Identities = 10/26 (38%), Positives = 14/26 (53%)

Query: 209 GELPLSLAACTKQWDVVSYLLENPHQ 234
G PL LA + W++V+ LL Q
Sbjct: 342 GRSPLILATASASWNIVNLLLSKGAQ 367

Score = 48 (22.3 bits), Expect = 3.2e-05, Sum P(5) = 3.2e-05Identities = 9/32 (28%), Positives = 20/32 (62%)

Query: 524 VMIQKVILRDLLRFLLIYLVFLFGFAVALVSL 555 +++ +VIL+ LLR ++++ L F ++ L Sbjct: 860 IVMLEVILKTLLRSTVVFIFLLLAFGLSFYIL 891

Score = 41 (19.0 bits), Expect = 2.7e-08, Sum P(6) = 2.7e-08 Identities = 9/28 (32%), Positives = 15/28 (53%)

Query: 525 MIQKVILRDLLRFLLIYLVFLFGFAVAL 552 +I K +LR + F+ + L F F + L Sbjct: 865 VILKTLLRSTVVFIFLLLAFGLSFYILL 892

Score = 40 (18.6 bits), Expect = 2.9e-07, Sum P(5) = 2.9e-07Identities = 13/50 (26%), Positives = 24/50 (48%)

Query: 620 MVLLLLLAYVLLTYILLLNMLIALMSETVNSVATDSWSIWKLQKAISVLE 669 +V + LL L++ +LLN+ S ++ ÷ T S + + S LE Sbjct: 875 VVFIFLLLAFGLSFYILLNLQDPFSSPLLSIIQTFSMMLGDINYRESFLE 924

Score = 40 (18.6 bits), Expect = 7.6e-05, Sum P(5) = 7.6e-05Identities = 8/19 (42%), Positives = 12/19 (63%)

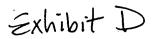
Query: 296 TPLKLAAKEGKIEIFRHIL 314 TPL LA + G +E+ + L Sbjet: 241 TPLHLAVQNGDLEMIKMCL 259

Score = 39 (18.1 bits), Expect = 2.7e-08, Sum P(6) = 2.7e-08 Identities = 7/19 (36%), Positives = 14/19 (73%)

Query: 625 LLAYVLLTYILLINMLIAL 643 L+++ + I+L+N+LI L Sbjct: 941 LVSFTIFVPIVLMNLLIGL 959

Score = 39 (18.1 bits), Expect = 6.8e-07, Sum P(6) = 6.8e-07 Identities = 9/36 (25%), Positives = 18/36 (50%)

Query: 293 QDLTPLKLAAKEGKIEIFRHILQREFSGLSHLSRKF 328 + LT L '+ +IE+ H + +E+ + L+ F Sbjet: 681 EPLTALNAMVQNNRIELLNHPVCKEYLLMKWLAYGF 716





# **Qualified Target Summary Sheet**

	Vanilloid Receptor Homologue
	(VR-2)
CFA Disease Area (s):	Pain
Druggable Target Class:	Calcium channel
MPI Gene Sequence Identifier:	Flh21e11 (Mine 18560)
Top Blast Hit:	Rat vanilloid receptor 1 (VR1)
Amino Acid Coding Region:	ORF: 361-2652
CDNA Length:	2806 bp
Source (Tissue / Cell Line):	First clone identified in an internal heart library
Novel / Unrecognized:	? Unrecognized / Novel
% Novelty:	66% novel across the complete cDNA. Hits unannotated sequence in Non-Public Patent Data Base
Patent Status:	Filed Nov. 1, 1998
Full Length Clone:	Yes
Expression Profiling Results:	Present in a sub-population of sensory neurons different from VR1.  Also present in sympathetic neurons.
The state of the s	
Background:	The published vanilloid receptor (Caterina et. Al. Nature 389:816-24, 1997) responds to heat and capsaicin by activating Ca++ influx in sensory neurons (Tominaga et.al., Neuron 21: 531-43, 1998). Capsaicin also binds to this channel.
Hypothesis:	This channel may be responsible for hypersensitivity in chronic neuropathic pain and represents a unique target for pain.
Assay Type:	Cell-based assay
Reagents Needed:	Open reading frame will be cloned by Millennium into pCDNA 3.1
Readout:	
Critical Experiments Necessary:	

MPI Target Name:

Vanilloid Receptor Homologue (VR-2)

**QT Nomination Date:** 

12/22/98

Acti n Tak n:

Date Accepted:

Accepted QT (unrecognized) Pending full length cDNA

Bay r QT Leader: MPI QT Leader:

Rory Curtis or Peter DiStefano